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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,291	02/05/2007	Tsvee Lapidot	30694/42021	6831

4743 7590 03/25/2009

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
03/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,291	LAPIDOT ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 26-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25* is/are rejected.

7)☒ Claim(s) *24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/15/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Examiner acknowledges the election, with traverse, of Group II (claims 17-25) directed to a population of cells, in the reply filed on 22 January 2009.

The applicant has traversed the restriction requirement. The applicant summarizes the traversal as "the issue is whether the currently pending claims are properly categorized into more or less than one combination of patentable categories specified by Rule 475(b)" (Remarks, page 3, last two lines). 37 CFR § 1.475(b) states:

> **(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:**
>
> (1) A product and a process specially adapted for the manufacture of said product; or
> (2) A product and process of use of said product; or
> (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
> (4) A process and an apparatus or means specifically designed for carrying out the said process; or
> (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

The applicant proceeds to describe the relationships between the 10 groups identified by the examiner (Remarks, pages 4-5). The applicant concludes "[t]he analysis described in the preceding paragraph[s] reveals that each of the ten claim Groups is drawn to a product, a process specially adapted for the manufacture of said product, or a use of said product…[which] falls within a single enumerated combination of categories under Rule 475(b)" (Remarks, page 5, last paragraph).

The examiner finds the applicant's conclusion flawed because the applicant's analysis shows that there are several products, each having at least one associated

method of use and/or manufacture. For example, the applicant indicates that Group VII is a product used in the method of Group VIII, while Group II is a product manufactured by the method of Group I. The examiner interprets the applicant's analysis as showing that two different products are being claimed and that each has a different type of method associated with the respective product. Therefore, all four of these groups (I, II, VII & VIII) cannot fit together into any of the categories described in Rule 475(b). Accordingly, the examiner finds the applicant's argument unpersuasive and reiterates his conclusion that the various inventions claimed in the instant application lack unity of invention.

Because the traversal is non-persuasive, the restriction is made final.

Claim Status

Claims 1-40 are pending. However, claims 1-16 and 26-40 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR § 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 26-34 and 38 are amended. Claims 17-25 are under current examination.

Oath/Declaration

The oath or declaration, having the signatures of all inventors, received on 5 February 2007 is in compliance with 37 CFR 1.63.

Information Disclosure Statement

The Information Disclosure Statements (IDS) filed on 15 February 2008 consisting of 6 sheets are in compliance with 37 CFR 1.97. Accordingly, examiner has considered the Information Disclosure Statements.

Priority

This application claims benefit as a 371 of PCT/IL04/01018 (filed 11/08/2004). This application also claims benefit from foreign application ISRAEL 158868 (filed 11/13/2003). The instant application has been granted the benefit date, 13 November 2003, from the foreign application, ISRAEL 158868.

Claim Objections

Claims 24-25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 24 and 25 are directed to limitations which do not affect the structure of the claimed [cell] population. Therefore, they fail to further limit the claim from which they depend.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "stem cells expressing a high amount of immature primitive progenitors." Specifically, it is unclear how stem cells can "express" progenitors because cells do not express other cell types. The metes and bounds of this phrase are unclear because the terminology used does not clearly set forth the property of the stem cell claimed.

Claim 18 recites the limitation "the population of stem cells" in the preamble. There is insufficient antecedent basis for this limitation in the claim, because antecedent claim 17 is directed to "a population" and not "a population of stem cells."

Claim 19 recites the limitation "the population of cells" in the preamble. There is insufficient antecedent basis for this limitation in the claim, because antecedent claim 17 is directed to "a population" and not "a population of cells."

The fact that both claims 18 and 19 depend from claim 17 and improperly attempt to provide antecedent basis to different types of populations, indicates that the metes and bounds of the instant claims is not clear.

Claim 23 recites "is about and above." MPEP2173.05(b) indicates the court held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). The examiner concludes that "is about and above" and "at least about" have the same indefinite meaning. Furthermore, the examiner concludes that claims 24-25 also have unclear recitations of ranges which seem to be encompassed by the "at least about" –type indefiniteness, particularly, "about and below" and "equal to or higher than about." Therefore, claims 23-25 should be amended to clarify the recited ranges.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17-25 are rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter. The phrase "stem cells" as defined by the specification at page 15, lines 9-11, states that the phrase "stem cells" refers to cells, which are capable of differentiation into other cell types having a particular specialized function (i.e., "fully differentiated" cells). Since the definition of "stem cells" is so broad, a skilled artisan would conclude that such a stem cell is present or is intended to be present in a human being, said cell becoming integrated into the human being and therefore being an inseparable part of the human itself. The scope of the claim(s), therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation of isolated or "non-human" would be remedial. See 1077 O.G. 24, April 21, 1987.

In addition, as a product by process, there is no requirement of the claim for the stem cells to maintain the sequence of CXCR4, thus the immature stem cell in a subject would be indistinguishable from that would be produced normally during a differentiation process into hematopoietic stem cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19 and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449).

Claim 17 is directed to a population comprising stem cells expressing a high amount of immature primitive progenitors, exhibiting improved CXCR4 signaling capability in response to low and/or high concentration of SDF-1, prepared by introducing into the stem cells a DNA fragment comprising the sequence of CXCR4. The structural limitations of claim 17 seem to be a [cell] population comprising stem cells having a DNA fragment comprising the sequence of CXCR4. Sawada et al. teach a transgenic mouse comprising a human CXCR4 gene (page 1440, Materials). The transgenic mouse comprises a cell population comprising stem cells having the CXCR4 gene.

Claim 18 is directed to the population of stem cells according to claim 17, wherein the stem cells are hematopoietic stem cells. The transgenic mouse of Sawada et al. comprises a cell population comprising hematopoietic stem cells having the CXCR4 gene.

Claim 19 is directed to the population of cells according to claim 17 or 18, being capable of differentiating towards the myeloid and erythroid lineages. Sawada et al.

indicate that immature myeloid and erythroid lineage cells are produced in their transgenic mice (page 1444, Fig.3).

Claims 24-25 are directed to limitations which affect the concentration of SDF-1. These claims to not further limit the structure of the [cell] population of claim 17. Therefore, the teachings of Sawada et al. satisfy the limitations of claims 24-25.

Accordingly, Sawada et al. anticipated the instant claims.

Claims 17-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Petit et al (Nature Immunology. July 2002; 3(7): 687-694, 787).

Claim 17 is directed to a population comprising stem cells expressing a high amount of immature primitive progenitors, exhibiting improved CXCR4 signaling capability in response to low and/or high concentration of SDF-1, prepared by introducing into the stem cells a DNA fragment comprising the sequence of CXCR4. as a product by process, there is no requirement of the claim for the stem cells to maintain the sequence of CXCR4, thus the immature stem cell in a subject would be indistinguishable from that would be produced normally during a differentiation process into hematopoietic stem cell. Therefore, the immature stem cells taught by Petit et al. anticipate the instant claim.

Claims 18-25 are similarly anticipated by the immature stem cells of Petit et al. because the structural limitations of the [cell] population is inherent to immature stem cells.

Accordingly, Petit et al. anticipated the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawada et al (J. Exp. Med., May 4, 1998; 187(9): 1439-1449) in view of Lapidot et al. (Leukemia. October 2002; 16(1): 1992-2003).

Claim 17 is directed to a population comprising stem cells expressing a high amount of immature primitive progenitors, exhibiting improved CXCR4 signaling capability in response to low and/or high concentration of SDF-1, prepared by introducing into the stem cells a DNA fragment comprising the sequence of CXCR4. The structural limitations of claim 17 are that the [cell] population comprising stem cells has a DNA fragment comprising the sequence of CXCR4. Sawada et al. teach a transgenic mouse comprising a human CXCR4 gene (page 1440, Materials). The transgenic mouse comprises a cell population comprising stem cells having the CXCR4 gene.

Claim 18 is directed to the population of stem cells according to claim 17, wherein the stem cells are hematopoietic stem cells. The transgenic mouse of Sawada et al. comprises a cell population comprising hematopoietic stem cells having the CXCR4 gene.

Claim 19 is directed to the population of cells according to claim 17 or 18, being capable of differentiating towards the myeloid and erythroid lineages. Sawada et al. indicate that immature myeloid and erythroid lineage cells are produced in their transgenic mice (page 1444, Fig.3).

Claims 24-25 are directed to limitations which affect the concentration of SDF-1. These claims to not further limit the structure of the [cell] population of claim 17. Therefore, the teachings of Sawada et al. satisfy the limitations of claims 24-25.

Sawada et al. does not explicitly teach the limitations of claims 21-23 wherein the population of cells comprises $CD34^{+}/CD38^{-/low}$ progenitor cells.

However, Lapidot teach cord blood contains primitive $CD34^+/CD38^{-/low}$ stem cells which are up to 5% of total $CD34^+$ cells. (page 1994, col.2). Therefore, Lapidot et al. indicate that $CD34^+/CD38^{-/low}$ cells are immature primitive progenitor cells (claim 21), which are about 1-5% of the population (claim 22) and are about and above 3% of the population (claim 23). Since the scope of the population is not precisely defined by the claims or specification, the examiner concludes that Lapidot teaches the ranges recited in the instant claims.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of Sawada and Lapidot to deduce that the cell populations of Sawada et al. contain $CD34^+/CD38^{-/low}$ transgenic stem cells comprising CXCR4.

The person of ordinary skill in the art would have been motivated to make those modifications because Lapidot et al. describe the transgenic mice of Sawada et al. which overexpress human CXCR4 as having hematopoietic stem cells. Lapidot et al. teach that mammals have a population of immature primitive progenitor cells in cord blood which are $CD34^+/CD38^{-/low}$ cells which are about 1-5% of the population. While not stating that the animals of Sawada et al. have $CD34^+/CD38^{-/low}$ cells which are transgenic for CXCR4 and which are about 1-5% of the population, there is strong suggestion that overexpressing CSCR4 has not altered the percentage of $CD34^+/CD38^{-/low}$ cells in the cord blood population of the transgenic mice.

The skilled artisan would have had a reasonable expectation of success in combining the teachings of Sawada et al. and Lapidot et al. because each of these teachings describe populations of cells from the Sawada transgenic mice.

Therefore the [cell] population as taught by Sawada et al. in view of Lapidot et al. would have been *prima facie* obvious over the [cell] population of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633